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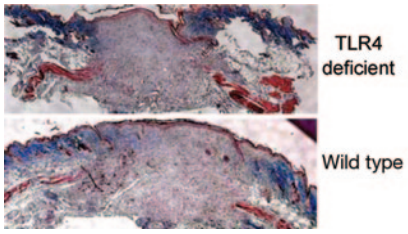
The Arsenal against Yeast

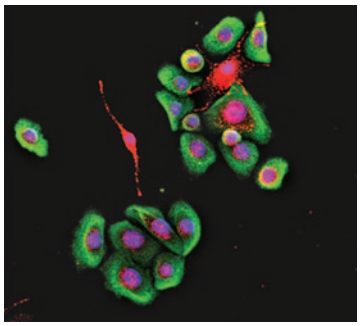
In addition to their fungicidal activity, antimicrobial agents provide apoptotic, antivirulence, and immunomodulatory functions for host cells. In the face of increasing antimycotic resistance, Wagener and colleagues discovered an antimicrobial human glyceraldehyde-3-dehydrogenase (hGAPDH) (2-32) peptide that is secreted by epithelial cells during mucosal candidiasis, binds to the yeast cell wall, induces apoptosis after internalization, and partially inhibits yeast protease activity. In addition, this peptide increases expression of immunomodulatory cytokines by the host and protects against tissue damage in an oral candidiasis model. These findings are promising for future combination treatments that target yeast cells from various directions. ***See page 144***

Early for Closure



Toll-like receptors (TLRs), which function in both innate and adaptive immune responses, have been implicated in various wound-healing situations. Chen and colleagues demonstrated that TLR4 expression is altered during wound healing and that TLR4 acts early in this process. Mice deficient in this factor exhibited alterations in IL-1β, IL-6, and epidermal growth factor as well as in infiltration of neutrophils, macrophages, and T cells in wounds. Finally, IL-1β production by keratinocytes in wounds is induced by TLR4 via the p38/JNK pathway. Together, these results indicate that TLR4 is an important player in wound inflammation and that TLR4 helps induce an optimal early inflammatory environment suitable for wound healing. ***See page 258***

Neighboring Effects



Wnt signaling is known to function in skin-pigmentation processes; however, the Wnt inhibitory factor-1 (WIF-1) is expressed only in keratinocytes and fibroblasts. Kim and colleagues explored the relationship between WIF-1 and pigmentation and found that downregulation of the *WIF-1* gene in neighboring keratinocytes and fibroblasts was associated with hyperpigmentation at the molecular level and with melasma. Furthermore, upregulation of *WIF-1* with recombinant human protein reduced pigmentation. Mechanistically, these effects of WIF-1 downregulation in neighboring cells are mediated by the stimulation of melanogenesis and melanosome transfer through the upregulation of Wnt via both the canonical and non-canonical pathways. ***See page 191***

Studying Minnesota

To accumulate population-based incidence data for hidradenitis suppurativa (HS), a chronic, recurrent inflammatory disorder of hair follicles in apocrine gland–bearing sites, Vazquez and colleagues examined 268 confirmed diagnoses of the 1,263 patients involved in the Rochester Epidemiology Project (REP) from 1968 to 2008. The incidence of HS was 6.0 cases per 100,000 individuals and appeared to rise with time. HS was associated with smoking, obesity, and gender, and disease severity was associated with gender and smoking. A high proportion of patients with this disabling disease condition exhibited depression. ***See page 97***

Head to the Lymph Nodes

Alterations in EGF expression are of prognostic relevance in melanoma; however, the effects of this pathway on metastasis to the lymph nodes have not been studied. Bracher and colleagues demonstrated that EGF directly stimulates lymphatic endothelial cells, induces vascular endothelial growth factor-C expression, and increases tumor motility. Because increased serum EGF was noted in melanoma patients with lymph node micrometastases, EGF may be useful as a prognostic marker to predict lymph node metastasis. This is important for therapy considerations because metastatic melanoma is life-threatening. ***See page 230***

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